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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/966,746	10/01/2001	Maurice Zauderer	1821.0060001/EKS/AJK	3613

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EXAMINER	
LUCAS, ZACHARIAH	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 07/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/966,746	ZAUDERER, MAURICE	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 1-7 are pending and under consideration in the present application.

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 17, 2004 has been entered.

Claim Rejections - 35 USC § 112

3. **(Prior Rejection- Maintained)** Claims 1-7 were rejected in the prior action under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims read on methods of screening for potential vaccines for infectious diseases comprising the steps of 1) identifying host cell gene products that are up-regulated during infection, and 2) screening said host cell gene products for immunogenicity. These claims are rejected because the applicant has not shown that the claimed method would be effective in identifying potential vaccines for any infectious disease.

The claims have been amended to require that the host cell gene products detected are upregulated by a factor of 9 or greater. The Applicant argues that gene products upregulated by

such an amount are more likely to be immunogenic. The Applicant traverses the rejection on the basis of the Declaration by Dr. Hunt, which presents that opinion that those in the art would be able to use the claimed methods to identify potential vaccine targets, and arguing that those in the art would have expected such self-target to be potential vaccine targets through analogy to the identification of anti-tumor antigens. These arguments are not found persuasive.

First, while each of the Veronese, the Hickman, and Herberts recognize that there are self-antigens that are upregulated during infection by certain pathogens, none of these references assert that such antigens would be potential vaccine targets. The Herberts reference, which comes closest to supporting the Applicant's assertion, indicates that the autoreactive T cells induced during such infections may be useful in clearance of the infection. Page 53. However, the reference also teaches that the role of such T cells is not understood, and warns that these cells may also be immunopathogenic, rather than helpful, to the host. Id. These teachings and warnings are supported by the teachings of Hickman (page 26, both stating the unknown consequences of the autoimmunity, but noting that it fits well in the development of pathogenic autoimmunity in certain infections -AIDS), and Veronese (page 23). Thus, while the art supports the assertion that there are immunogenic self-antigens that are upregulated upon infection, they do not provide a clear basis for the assertion that such antigens would be effective as vaccine targets. Thus, in view of the uncertainty in the art, the lack of working examples, and the limited guidance in differentiating between vaccine targets and targets of pathogenic autoimmunity, the Applicant's assertions are not found persuasive.

The amendment of the claims to indicate the gene products must be upregulated by a factor of 9 or greater is also not found persuasive. While this may, as argued by the Applicant,

increase the likelihood that the gene product would be capable of inducing an immune response in the host, it does not demonstrate that the indicated gene products would be useful in the treatment of an infectious disease, or that responses against such products would not induce the immunopathogenic responses suggested by Herberts.

While the Declaration asserts analogy between the art of anti-tumor vaccination and the present invention, it is noted that the art has established anti-tumor efficacy, but has found only pathogenic autoimmunity with respect to immune responses to self-antigens, as in the case of HIV. As indicated by the Applicant, the Veronese reference does indicate that CTL responses may be useful in the control of viral spread and infection. However, the reference indicates that these responses are HIV-1-specific, and provides no information as to whether such responses to self-antigens would be so useful, or would lead to enhanced immuopathogenicity as suggested by Herberts and Hickman.

Further, while the Office accepts that the art has demonstrated certain instances where induction of a anti-self response has been effective against tumors, the closest art relating to the presently claimed invention has not only failed to demonstrate that such an immune response would be useful against an infectious disease, but has stated that it is uncertain whether such a response would be helpful or immunopathogenic in the host.

It is further noted that the Declaration is not commensurate in scope with the claims. Whereas the Declaration argues that antigens that are expressed on cell surfaces as part of an MHC complex are evidence that the proteins are at least antigenic, the claims read on the up-regulation of any protein, whether expressed on the cell surface alone, or part of an MHC complex. Further, the claims are not limited to proteins that are expressed on the cell, but to any

protein that is upregulated, including secreted proteins. Thus, even if the Declaration was found persuasive with respect to the arguments presented therein, the scope of the claims exceeds the scope of the arguments presented.

For the reasons above, and the reasons of record, the rejection is maintained.

4. **(New Rejection)** Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, if it is assumed that the Applicant is enabled for methods wherein the step of screening for immunogenicity entails screening for the ability to induce a response in the host organism against the cell expressing said gene products, does not reasonably provide enablement for methods wherein the step involves only screening for immunogenicity in general. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The claims have been described in part above, and in the prior actions. They include steps of identifying host-cell gene products upregulated during infection and "screening said host cell gene products for immunogenicity." Neither the claims nor the specification provide any limits on what is meant by the indicated screening step.

The specification teaches that the concern of the claimed method is the identification of host cell gene products that are upregulated upon host cell infection, and the identification of such gene products that are useful in inducing an immune response such that the infection will be treated. See, App. page 1, pages 2-3. Additionally, Applicant's arguments in the Response, and in the Declaration, indicate that it is the ability of the host cell gene product to induce an immune response in the host organism that determines whether the antigen is likely to be a potential

vaccine target. See, Response, pages 4-5; and Dec. pages 2-3. Thus, if the claimed method were found to be enabled, it would be for embodiments where the up-regulated self-antigen is capable of inducing an immune response in the host organism.

The claims, however, do not require that the identified gene products be screened for the ability to induce an immune response in the host organism. Rather, they indicate that the gene product is screened for immunogenicity in general. However, the ability of a peptide to induce any immune response in any system is not sufficient to demonstrate the ability of the peptide to induce an immune response in the host organism such that the peptide may be used as an effective vaccine against host-cell infection. The art recognizes that immune tolerance to self-antigens is an obstacle to inducing immune responses against self-antigens. See e.g., Hernández et al. (PNAS 99:12275-80, page 12275 paragraph spanning left and right columns. Thus, it is not the ability of the identified gene products to be immunogenic in general that is required to recognize vaccine targets in the claimed method. Further, the Declaration, the application, and the art cited therein indicate that, if such self-antigens are useful in the treatment of infections, it is through the induction of host CTL responses against the infected cells. See e.g., Declaration, pages 2-3; App., page 13 lines 4-5, and page 14; Veronese, abstract and page 2509; and Herberts, page 53. From the context presented in the Applicant's arguments, and the teachings of the art and the specification, it appears that host cell gene products must not only be immunogenic, but must also be capable of inducing an immune response in the host organism against the infected cells.

For the reasons above, the claimed methods are rejected as not corresponding in scope to the invention as described by the Applicant. Because the art and arguments presented by the

Applicant indicate that additional limitations are required to make the claimed invention operative, the claims are rejected because the claimed step of "screening said host cell gene products for immunogenicity" does not alone appear to represent an operative embodiment of the claimed invention.

Conclusion

5. No claims are allowed.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner

James C. Housel 7/12/04

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